

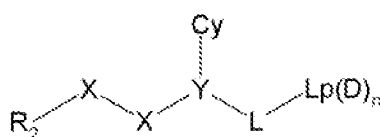
**Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1 to 35 (canceled):

36 (previously presented): A process for the preparation of serine protease inhibitor compound of formula (I)



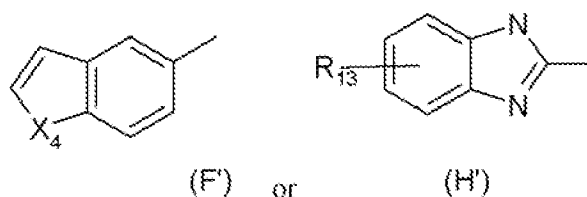
(I)

wherein:

R<sub>2</sub> is:-

- (i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido (CONH<sub>2</sub>), aminoalkyl, alkoxy or alkylthio;
- (ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub> and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;
- (iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;
- (iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;
- (v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

- (vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;
- (vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydro-imidazo[1,2-a]pyrimidin-2-yl;
- (viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;
- (ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;
- (x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;
- (xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;
- (xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;
- (xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ; or
- (xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;
- with the proviso that  $R_2$  cannot be aminoisoquinolyl;
- or  $R_2$  is a group of formula (F') or (H')



wherein  $X_4$  is O or S, and  $R_{13}$  is selected from hydrogen, fluoro, chloro and methyl;

-X-X- is -CONH-;

$R_1$  is hydrogen, hydroxy, alkoxy, alkyl, alkylaminoalkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

$R_{1j}$  is hydrogen, hydroxy, alkoxy, alkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

Y is a CH group;

Cy is an optionally  $R_{3a}$  substituted: phenyl group, or a phenyl group substituted by  $R_{3i}X_i$ ;

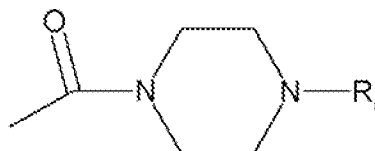
each  $R_{3a}$  independently is hydrogen, hydroxyl, alkoxy, aralkyloxy, alkyl, alkylaminoalkyl, hydroxymethyl, carboxy, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, aminomethyl,  $CONH_2$ ,  $CH_2CONH_2$ , (1-6C)alkanoylamino, alkoxycarbonylamino, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkylloxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S; and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or  $-OCH_2O-$  which is bonded to two adjacent ring atoms in Cy;

$X_i$  is a bond, O, NH or  $CH_2$ ;

$R_{3i}$  is phenyl, pyridyl or pyrimidinyl optionally substituted by  $R_{3a}$ ;

and

$-L-Lp(D)_n$  is of the formula:



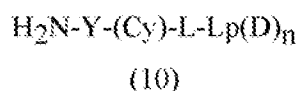
in which  $R_f$  is  $-(CH_2)_c-R_c$ ,  $-CHR_eR_f$ ,  $-CH_2-CHR_eR_f$ ,  $-CH_2-CH_2-CHR_eR_f$ , or  $R_g$  in which c is 1 or 2;  $R_c$  is thienyl, thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, (1-4C)alkoxycarbonyl, carboxy, acetylamino, chloro, fluoro, cyano, (1-3C)alkyl, trifluoromethyl, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl (which may bear a methyl, methylamino, dimethylamino, carboxy, dialkylaminosulphonyl, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl,

alkylaminocarbonyl, amino, amido, alkoxycarbonyl, acetylamino, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent); each of  $R_E$  and  $R_F$  independently is hydrogen or  $C_{1-3}$ alkyl; or  $CHR_E R_F$  is cyclopentyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), cyclohexyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), piperidin-4-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), or indan-2-yl; and  $R_G$  is  $\lambda^6$ -1,1-dioxobenzo[b]thiophen-7-yl;

or a physiologically-tolerable salt thereof;

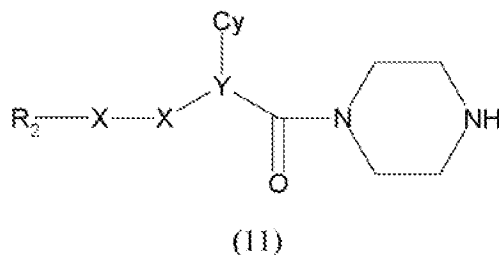
which process comprises

- (a) reacting a compound of formula (10)

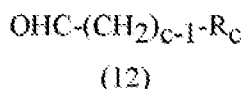


with a compound of formula  $R_2-COOH$ , under amide bond-forming conditions; or

- b) when  $R_F$  is  $-(CH_2)_c-R_C$ , reacting a compound of formula (11)



with a compound of (12)



in the presence of a reducing agent;

followed if a salt is required, by forming a physiologically acceptable salt.

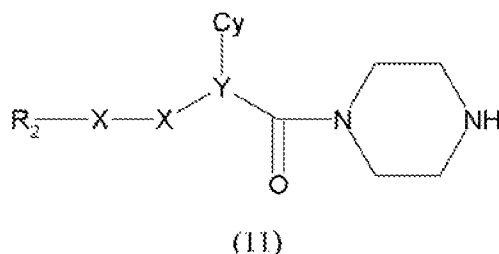
37 (previously presented): A process as claimed in Claim 36, in which the compound of formula (I) is selected from:

1-(Indole-6-carbonyl-D-phenylglyciny)-4-[2-(4-pyridinyl)ethyl]piperazine;

1-(3-Chloroindole-6-carbonyl-D-phenylglycyl)-4-[2-(4-pyridinyl)ethyl]piperazine;  
 1-(4-Methoxybenzoyl-D-phenylglycyl)-4-(1-methylpiperidin-4-yl)piperazine;  
 1-(Indole-6-carbonyl-D-phenylglycyl)-4-(1-methylpiperidin-4-yl)piperazine;  
 1-(4-Methoxybenzoyl-D-(2-chlorophenyl)glycyl)-4-(1-methylpiperidin-4-yl)piperazine;  
 1-(Indole-6-carbonyl-D-(2-chlorophenyl)glycyl)-4-(1-methylpiperidin-4-yl)piperazine; and  
 1-(4-Methoxybenzoyl-D-(2-trifluoromethylphenyl)glycyl)-4-(1-methylpiperidin-4-yl)-  
 piperazine;  
 and physiologically-tolerable salts thereof.

38-39 (cancelled):

40 (previously presented): A compound of formula (11)

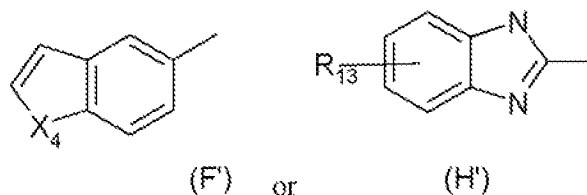


in which:

$R_2$  is:-

- (i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy,  $\text{MeSO}_2$ - or  $R_{1j}$ , and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido ( $\text{CONH}_2$ ), aminoalkyl, alkoxy or alkylthio;
- (ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$  and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;
- (iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;
- (iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

- (v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;
- (vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;
- (vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;
- (viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;
- (ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;
- (x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;
- (xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;
- (xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;
- (xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>; or
- (xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;
- with the proviso that R<sub>2</sub> cannot be aminoisoquinolyl;
- or R<sub>2</sub> is a group of formula (F') or (H')



wherein X<sub>4</sub> is O or S, and R<sub>13</sub> is selected from hydrogen, fluoro, chloro and methyl;

-X-X- is -CONH-;

R<sub>1</sub> is hydrogen, hydroxy, alkoxy, alkyl, alkylaminoalkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

R<sub>1j</sub> is hydrogen, hydroxy, alkoxy, alkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

Y (the  $\alpha$ -atom) is a CH group;

Cy is an optionally R<sub>3a</sub> substituted: phenyl group, or a phenyl group substituted by R<sub>3i</sub>X<sub>i</sub>;

each R<sub>3a</sub> independently is hydrogen, hydroxyl, alkoxy, aralkyloxy, alkyl, alkylaminoalkyl, hydroxymethyl, carboxy, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, aminomethyl, CONH<sub>2</sub>, CH<sub>2</sub>CONH<sub>2</sub>, (1-6C)alkanoylamino, alkoxycarbonylamino, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkylloxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula -C(X<sup>3</sup>)N(R<sup>11</sup>)R<sup>12</sup> (wherein X<sup>3</sup> is O or S; and R<sup>11</sup> and R<sup>12</sup> are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or -OCH<sub>2</sub>O- which is bonded to two adjacent ring atoms in Cy;

X<sub>i</sub> is a bond, O, NH or CH<sub>2</sub>; and

R<sub>3i</sub> is phenyl, pyridyl or pyrimidinyl optionally substituted by R<sub>3a</sub>.

41-46 (canceled);